

EXHIBIT 16

141: Zhonghua Jie He He Hu Xi Za Zhi. 2002 Jun;25(6):337-40. [Related Articles](#), [Links](#)

[The pathogenic role of macrophage migration inhibitory factor in acute respiratory distress syndrome]

[Article in Chinese]

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OBJECTIVE To investigate the expression and pathogenic role of macrophage migration inhibitory factor(MIF) in human acute respiratory distress syndrome(ARDS)
METHODS The serum level of MIF in ARDS patients and normal persons were measured by ELISA method. Peripheral blood mononuclear cell (PBMC) MIF expression was determined by flow- cytometry. The expression of MIF mRNA and protein in the lung tissues were detected by using double immuno histochemistry labeling and in situ hybridization. **RESULTS** The serum level of MIF increased significantly in ARDS patients as compared with normal persons ($P < 0.01$). The percentage of PBMC MIF expression was higher in ARDS patients than in normal controls ($P < 0.01$). In situ hybridization and immunohistochemistry showed undetectable or weak MIF mRNA and protein expression in normal lungs. In contrast, there was marked upregulation of MIF mRNA and protein expression in the ARDS lungs. In ARDS macro phages infiltrated the alveolar space and interstitium, most of which also expressed MIF. Infiltrating macrophages were almost restricted to the areas of severe tissue damage. The MIF expression level showed a strong correlation with the number of infiltrating macrophages. **CONCLUSIONS** The serum level of MIF and PBMC MIF expression increased in ARDS patients with enhanced pulmonary MIF expression and macrophage infiltration, which suggests that MIF plays a pivotal role in the pathogenesis of ARDS.

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